I

104TH CONGRESS
1ST SESSION

H. R. 1742

To amend the Federal Food, Drug, and Cosmetic Act to revise the process for the approval of drugs and for other purposes.

IN THE HOUSE OF REPRESENTATIVES

JUNE 6, 1995

Mr. WYDEN introduced the following bill; which was referred to the Committee on Commerce

---

A BILL

To amend the Federal Food, Drug, and Cosmetic Act to revise the process for the approval of drugs and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; REFERENCE; TABLE OF CONTENTS.

(A) SHORT TITLE.—This Act may be cited as the ''FDA Modernization Act of 1995''.

(b) REFERENCE.—Whenever in this Act an amendment or repeal is expressed in terms of an amendment to, or repeal of, a section or other provision, the reference

shall be considered to be made to a section or other provision of the Federal Food, Drug, and Cosmetic Act.

(c) TABLE OF CONTENTS.—The table of contents of this Act is as follows:

Sec. 1. Short title; reference; table of contents.
Sec. 2. Findings.
Sec. 3. Responsibility of the Secretary.
Sec. 4. Conditional approval.
Sec. 5. Use of institutional review boards.
Sec. 6. Review by independent testing organizations.
Sec. 7. Limitations on authority over legitimate labeling and advertising.
Sec. 8. Review by expert advisory panel.
Sec. 9. Rationalizing good manufacturing practices.
Sec. 10. Export of drugs and devices.
Sec. 11. Regulation of biological products.
Sec. 12. Initial reporting of devices.
Sec. 13. FDA response to G.M.P. violations.

SEC. 2. FINDINGS.

The Congress finds the following:

(1) The Food and Drug Administration has primary responsibility to ensure the safety and effectiveness of drugs and medical devices.

(2) Within the scope of that mission, the Food and Drug Administration also has a public mandate to help speed the introduction of life-saving and life-enhancing new products to the marketplace.

(3) The United States medical products industry is a nationally important employer, and a major, positive balance-of-trade factor in our economy.

(4) It is apparent to persons both within and outside of the agency that certain Food and Drug

Administration practices, policies, and systems may—

(A) needlessly delay the introduction of new products,

(B) withhold new health care benefits to American citizens,

(C) erode job development in an important United States industry, and

(D) reduce our effective competitiveness in international markets.

(5) These problems are compounded by the twin pressures of an increasing agenda of regulatory mandates for which the Food and Drug Administration has been made responsible, and budget limitations which have restricted the agency's ability to properly address all functions in an expeditious manner.

(6) The agency is hamstrung by some regulatory processes which are outdated, and by systems, policies, technical knowledge, and philosophies which have not, in every case, kept up with revolutionary changes in the underlying science now creating 21st century drug and medical device breakthroughs. Among other problems, these policies and philosophies may unnecessarily restrict the appropriate and

free flow of credible scientific knowledge between clinicians, researchers, and manufacturers.

(7) Better health care for all Americans is the ultimate goal as the Food and Drug Administration is reshaped to meet the challenges of regulating a rapidly growing, and changing, health care products industry.

SEC. 3. RESPONSIBILITY OF THE SECRETARY.

Section 903(b)(2) (21 U.S.C. 393(b)(2)) is amended by redesignating subparagraphs (A), (B), (C), (D), and (E) as subparagraphs (B), (C), (D), (E), and (F), respectively and by adding before subparagraph (B) (as so redesignated) the following:

''(A) consistent with the public health, rapidly making decisions on the approval of drugs and devices in accordance with this Act and biological products in accordance with section 351 of the Public Health Service Act;''.

SEC. 4. CONDITIONAL APPROVAL.

(a) DRUGS AND BIOLOGICAL PRODUCTS.—Section 505 (21 U.S.C. 355) is amended by adding at the end the following:

''(n) A new drug to treat life-threatening or serious conditions for which an application has been submitted under subsection (b) may, if the new drug is otherwise

approvable, receive a conditional approval on the basis of valid scientific evidence demonstrating a reasonable assurance of safety and effectiveness. A conditional approval shall become a final section 505 approval unless conditions set forth in such approval have not been met within a time certain as set by the Secretary in consultation with the applicant. If such conditions have not been fulfilled within such time, the conditional approval shall terminate. A new drug which has a conditional approval shall for purposes of this Act be considered an approved new drug. A conditional approval shall terminate upon the expiration of the period applicable to such approval.''.

(b) MEDICAL DEVICES.—Section 515 (21 U.S.C 360e) is amended by adding at the end the following:

''CONDITIONAL APPROVAL

''(j) A a class III device to treat life-threatening or serious health conditions for which an application for premarket approval has been submitted under subsection (c) may, if the device is otherwise approvable, receive a conditional approval on the basis of valid scientific evidence demonstrating a reasonable assurance of safety and effectiveness. A conditional approval shall be for such period as the Secretary designates in granting such approval. A device which has a conditional approval shall for purposes of this Act be considered an approved device. A conditional

approval shall terminate upon the expiration of the period applicable to such approval.''.

SEC. 5. USE OF INSTITUTIONAL REVIEW BOARDS.

(a) APPROVAL OF I.N.D. FOR DRUGS.—Section 505(i) (21 U.S.C. 355(i) is amended by inserting ''(1)'' after ''(i)'' and by adding at the end the following:

''(2)(A) An application (including an amendment or supplement thereto) for an exemption for a new drug for investigational use shall be deemed approved on the 30th day after the submission of the application to the Secretary unless on or before such day—

''(i) the Secretary, or

''(ii) the Secretary acting upon the recommendation of an institutional review board certified under paragraph (3)(C),

by order disapproves the application and notifies the applicant in writing of the disapproval and the reasons for disapproval and affords the applicant an opportunity for an informal hearing on the disapproval.

''(B) Personnel of the Secretary shall meet with any person who wishes to submit an application for a drug under paragraph (1) for the purpose of reaching agreement on the design and size of clinical trials in order to facilitate expeditious review of an application under subsection (b). Meetings shall be held within 30 days of any

reasonable request therefor. Minutes of any such meeting shall be exchanged.''.

(b) INVESTIGATIONAL DEVICES.—Section 520(g)(4)(A) (21 U.S.C. 360j(g)(4)(A)) is amended by striking ''unless'' and all that follows and inserting ''unless on or before such day—

''(i) the Secretary, or

''(ii) the Secretary acting upon the recommendation of an institutional review board certified under section 505(i)(3)(C),

by order disapproves the application and notifies the applicant in writing of the disapproval and the reasons for disapproval and affords the applicant an opportunity for an informal hearing on the disapproval. Personnel of the Secretary shall meet with any person who wishes to submit an application for a device under paragraph (1) for the purpose of reaching agreement on the design and size of clinical trials in order to facilitate expeditious review of an application under section 515(c). Meetings shall be held within 30 days of any reasonable request therefor. Minutes of any such meeting shall be exchanged.''.

(c) REVIEW OF CERTAIN CLINICAL INVESTIGATIONS.—Section 505(i) (21 U.S.C. 355(i), as amended by subsection (a), is amended by adding at the end the following:

''(3)(A) The Secretary shall use institutional review boards, approved by the Secretary, to review and approve the initiation and conduct of Phase I clinical investigations under paragraph (1). The Secretary shall certify an institutional review board as qualified to review and approve a Phase I clinical investigation upon a determination that the board meets the criteria established under subparagraph (C).

''(B)(i) The Secretary shall require private sponsors to submit proposed Phase I clinical investigations to be conducted under an exemption under this subsection to an institutional review board certified under subparagraph (A) in lieu of submission to the Secretary.

''(ii) The Secretary may, upon request, authorize commercial sponsors to submit proposed Phase I clinical investigations to be conducted under an exemption under this subsection to an institutional review board certified under subparagraph (A) in lieu of submission to the Secretary.

''(C) The Secretary, acting through the Commissioner of Food and Drugs and the Director of the National Institutes of Health, shall establish criteria for certification by the Commissioner of institutional review boards as qualified to approve the initiation and conduct of Phase I clinical investigations. Applicants shall apply to a cer-

tified institutional review board for approval to conduct a Phase I clinical investigation.

''(D) An institutional review board may approve a Phase I clinical investigation if it determines the investigation meets the requirements of paragraph (1) and is to be conducted in accordance with standards which provide reasonable protection of human subjects, including informed consent procedures.

''(E) For purposes of this paragraph, the term 'Phase I clinical investigations' means one or more clinical investigations that involve the introduction of an investigational new drug into human beings. Such an investigation shall be designed to determine parameters such as the following: the safety profile of the drug, the metabolism and pharmacologic actions of the drug in humans, the side effects associated with increasing doses of the drug, early evidence of effectiveness of the drug, and information about the drug's rate and extent to absorption.

''(4)(A) The Secretary (or an institutional review board with respect to a Phase I clinical investigation which it has approved) may place a clinical hold on any proposed or ongoing clinical investigation if the Secretary determines that such action is necessary for the protection of human subjects or that the clinical investigations are poorly supervised or executed, produce inaccurate or materially

insufficient data, or are based on clearly deficient protocols.

''(B) If an institutional review board places a clinical hold on an investigation under subparagraph (A), it shall immediately notify the Secretary of such action.

''(5)(A) Information otherwise protected from disclosure to the public under section 301(j) or 520(c) may be disclosed, under such conditions as the Secretary may specify, to members of an institutional review board and its staff if, in the opinion of the Secretary, such disclosure is necessary to protect the public safety and for the satisfactory performance by the institutional review board of its functions under paragraph (3).

''(B) The Secretary shall, in writing, require as a condition to the disclosure of information under this paragraph that the person receiving such information take such security precautions respecting the information as the Secretary shall by regulation prescribe. Disclosure by such person of such information to a person not authorized to receive it shall constitute a violation of section 301(j) and of section 1905 of title 18, United States Code.

''(6)(A) Any member of an institutional review board certified by the Secretary under paragraph (3)(C) shall, by reason of the member's performance of any duty, function, or activity required of, or authorized to be under-

taken by, the institutional review board under this subsection, be considered to be an employee of the Government under section 2671 of title 28, United States Code.

''(B) Any personnel of a hospital, university, or other institution under which an institutional review board certified by the Secretary under paragraph (3)(C) was organized shall, by reason of the personnel's performance of any duty, function, or activity required of, or authorized to be undertaken by, the institutional review board under this subsection, be considered to be an employee of the Government under section 2671 of title 28, United States Code.

''(7) The Secretary may make grants to institutional review boards to defray, in whole or in part, the costs associated with the approval of Phase I clinical investigations.''.

(b) REPORT.—Not later than the expiration of 5 years from the date of the enactment of this Act, the Secretary of Health and Human Services shall report to the Congress on the use the Secretary has made under paragraphs (3) through (7) of section 505(i) of the Federal Food, Drug, and Cosmetic Act of institutional review boards and any difficulties the Secretary has encountered in using such boards.

(c) EFFECTIVE DATE.—The amendments made by subsections (a), (b), and (c) with respect to review of clinical investigations under section 505(i) of the Federal Food, Drug, and Cosmetic Act by institutional review boards shall take effect upon the expiration of 36 months after the date of the enactment of this Act

SEC. 6. REVIEW BY INDEPENDENT TESTING ORGANIZATIONS.

(a) AMENDMENT.—Chapter IX is amended by adding after section 905 (21 U.S.C. 395) the following:

''PRIVATIZATION OF APPROVAL FUNCTIONS

''SEC. 906. (a) The Secretary, acting through the Commissioner of Food and Drugs, may establish and implement a program under which the Commissioner will contract, in whole or in significant part, with individuals and laboratories certified under subsection (b) to conduct, under such conditions as the Secretary may specify to assure unbiased scientifically valid results, the following activities and responsibilities of the Food and Drug Administration in connection with the approval of drugs and devices under sections 505 and 515 and with reviewing notifications required under section 510(k) and making written recommendations of initial classification under section 513(f)(1) of devices:

''(1) Toxicology reviews to determine if applicable requirements are being met.

''(2) Chemistry reviews to determine if applicable requirements are being met.

''(3) Statistical analysis to determine if applicable requirements are being met.

''(4) Preapproval manufacturing practice inspections to determine if applicable requirements are being met.

''(5) Any other function of the Food and Drug Administration relating to the review and approval of drugs or devices that the Secretary determines can be adequately performed under contract with qualified individuals and laboratories.

''(b) The Secretary, acting through the Commissioner of Food and Drugs, shall certify individuals and laboratories as qualified to carry out the functions described in paragraphs (1) through (6) of subsection (a) under a contract with the Commissioner of Food and Drugs.

''(c)(1) Information otherwise protected from disclosure to the public under section 301(j) or 520(c) may be disclosed to—

''(A) contractors certified under subsection (b), and

''(B) employees of such contractors,

if, in the opinion of the Secretary, such disclosure is necessary for the satisfactory performance by the contractor of work under a contract under subsection (a).

''(2) The Secretary shall, in writing, require as a condition to the disclosure of information under paragraph (1) that the person receiving such information take such security precautions respecting the information as the Secretary shall by regulation prescribe. Disclosure by such person of such information to a person not authorized to receive it shall constitute a violation of section 301(j) and of section 1905 of title 18, United States Code.

''(e) The review of an application for approval of a new drug or device under this Act or a biological product under section 351 of the Public Health Service Act shall not include the review of the environmental impact of such drug, device, or biological product under the Environmental Quality Improvement Act of 1970 (42 U.S.C. 4371 et seq.).''.

(b) REPORT.—Not later than the expiration of one year from the date of the enactment of this Act, the Secretary of Health and Human Services shall report to the Congress on—

(1) the use the Secretary has made under section 906 of the Federal Food, Drug, and Cosmetic Act of the authority to contract for individuals and

laboratories to perform duties of the Food and Drug Administration, and

(2) any difficulties encountered in contracting under such section 906.

SEC. 7. LIMITATIONS ON AUTHORITY OVER LEGITIMATE LABELING AND ADVERTISING.

(a) SECTION 201(m).—Section 201(m) (21 U.S.C. 321(m)) is amended to read as follows:

''(m)(1) The term 'labeling' means all labels and other written, printed, or graphic material upon any article or any of its containers or wrappers, or accompanying any such article.

''(2) Such term does not include scientifically valid—

''(A) reprints of articles published in peer-reviewed scientific publications, other generally recognized scientific materials such as medical textbooks, official compendia, abstracts and proceedings of scientific meetings, or information concerning decisions about drug utilization review or formulary decisions if—

''(i) such reprints, materials, or information are disseminated in a meeting to health professionals or to persons involved in the insurance of, or reimbursement for, drugs and de-

vices approved under this Act and section 351 of the Public Health Service Act, and

''(ii) the dissemination of such reprints, materials, or information was not required, directly or indirectly, by a pharmaceutical company or device manufacturer as a condition of financial support of the development of such materials or of such meeting;

''(B) materials used to fulfill the disclosure requirements of the Securities and Exchange Commission; or

''(C) other information intended primarily for distribution to shareholders (and potential shareholders);

if such information is reported to the Secretary at least 60 days before its dissemination.

''(3) If labeling contains information described in paragraph (2)(A) along with related data as may be deemed appropriate by the Secretary, the Secretary may require that persons disseminating such labeling include in the labeling a statement prescribed by the Secretary concerning such information if the Secretary finds that the information is scientifically insufficient, inaccurate, or misleading.''.

(b) SECTION 201(n).—Section 201(n) (21 U.S.C. 321(n)) is amended—

(1) by inserting ''(1)'' after ''(n)''; and

(2) by inserting the following at the end thereof:

''(2) For purposes of this subsection, the term 'advertising' does not include scientifically valid—

''(A) reprints of articles published in peer-reviewed scientific publications, other generally recognized scientific materials such as medical textbooks, official compendia, abstracts, and proceedings of scientific meetings, or information concerning decisions about drug utilization review of formulary decision if—

''(i) such reprints, materials, or information are disseminated in a meeting to health professionals or persons involved in the insurance of, or reimbursement for, drugs and devices regulated under this Act and section 351 of the Public Health Service Act, and

''(ii) the dissemination of such reprints, materials, or information was not required, directly or indirectly, by a pharmaceutical company or device manufacturer as a condition of

financial support of the development of such materials or of such meeting;

''(B) materials used to fulfill the disclosure requirements of the Securities and Exchange Commission or the Securities Act of 1933 and the Securities Exchange Act of 1934 and regulations promulgated thereunder; or

''(C) other information intended primarily for distribution to shareholders (and potential shareholders);

if such information is reported to the Secretary at least 60 days before its dissemination.

''(3) If advertising contains information described in paragraph (2)(A) along with related data as may be deemed appropriate by the Secretary, the Secretary may require that persons disseminating such advertising include in the advertising a statement prescribed by the Secretary concerning such information if the Secretary finds that the information is scientifically insufficient, inaccurate, or misleading.''.

(c) SECTION 201(p).—Section 201(p)(1) (21 U.S.C. 321(p)(1)) is amended by striking ''labeling thereof'' and inserting ''drug's labeling (as defined in paragraph (m))''.

(d) SECTION 502(a).—Section 502(a) (21 U.S.C. 352(a)) is amended by inserting ''(1)'' after ''(a)'' and inserting at the end thereof the following:

''(2) The Secretary does not have authority to require approval of promotional labeling prior to use or dissemination of such labeling. This paragraph does not apply to the regulation of tobacco products.

''(3) The dissemination of scientifically valid information as defined in section 201(m)(2)(A) is not a violation of this section, provided that (a) it is reported to the Secretary 60 days prior to dissemination, and (b) subject to provisions of Section 201(m)(3).''

(e) SECTION 502(n).—The first sentence of section 502(n) (21 U.S.C. 352(n) is amended by striking '', and (B)'' and inserting before the period at the end the following: '', and (C) no advertising shall be subject to approval prior to use or dissemination''.

(f) APPLICATION.—The amendments made by this section apply to the labeling and advertising of drugs, biological products, and devices which have been approved for at least one indication.

SEC. 8. REVIEW BY EXPERT ADVISORY PANEL.

Chapter IX is amended by adding at the end the following:

''REVIEW BY EXPERT ADVISORY PANEL

''SEC. 906. (a)(1) In the case of—

''(A) any person who has submitted an application under section 505(a) for approval of a new drug, or

''(B) any person who has submitted a product license application for a biological product under section 351(a) of the Public Health Service Act,

which the Secretary determines is to be used for the purpose of treating a serious or life-threatening disease or other health condition, such person (hereinafter in this section referred to as the 'applicant') may, not sooner than 90 days after submitting such application, request review of such application by an expert advisory panel under this section.

''(2) If an expert advisory panel appointed by the Secretary under subsection (b) recommends under subsection (d) that the drug reviewed should be approved under section 505 or that the biological product reviewed should have a product license issued for it under section 351 of the Public Health Service Act, then, within 45 days of receipt of the recommendation, the drug shall be deemed approved or the biological product shall be deemed to have a product license issued for it unless the Secretary determines that the applicant has not met standards of section 505 or 351, whichever is applicable.

''(b)(1) The Secretary may appoint expert advisory panels for review of applications under this section according to the various fields of clinical medicine and fundamental sciences in which drugs or biological products are used.

''(2)(A) Members of an advisory panel shall be selected from a list of persons submitted to the Secretary under subsection (e), and the Secretary shall designate the chairperson of each panel. Each advisory panel shall consist of 5 or more persons with training and experience in the fields of medicine and science applicable to the drug which is the subject of the application to be reviewed and who are otherwise qualified to review such applications.

''(B) Members of advisory panels appointed under this subsection shall be compensated at a rate not to exceed the daily equivalent of the rate in effect for GS–18 of the General Schedule for each day (including travel time) they are engaged in the performance of their duties as members of the advisory panel. All members, while so serving away from their homes or regular places of business, may be allowed travel expenses, including per diem in lieu of subsistence, in the same manner as such expenses are authorized by section 5703, title 5, United States Code, for employees serving intermittently.

''(c)(1) The Secretary shall, within 60 days of the receipt of a request under subsection (a)(1), refer an eligible application to an advisory panel, appointed under subsection (b), for the purpose of reviewing such application and shall provide to the panel such information as the Secretary determines will facilitate review of such application by the panel.

''(2)(A) Information provided under paragraph (1) which is otherwise protected from disclosure to the public under section 301(j) or 520(c) shall be disclosed to members of advisory panels only under the conditions specified in subparagraph (B).

''(B) The Secretary shall, in writing, require as a condition to the disclosure of information under subparagraph (A) that the person receiving it take such security precautions respecting the information as the Secretary shall by regulation prescribe. Disclosure by such person of such information to a person not authorized to receive it shall constitute a violation of section 301(j) and of section 1905 of title 18, United States Code.

''(d)(1) Within 60 days of the date information is provided to the expert advisory panel under subsection (c)(1), the expert advisory panel shall complete its review of the information received under subsection (c) with respect to an application being reviewed by the panel and

shall submit to the Secretary and the applicant a recommendation as to whether the drug included in the application should be approved in accordance with section 505 or whether a product license should be issued under section 351 of the Public Health Service Act for the biological product included in the application. A recommendation for approval of the drug or issuance of a license for a biological product shall specify the indication for which the drug or biological product is recommended for approval.

''(2) A summary of the recommendation submitted to the Secretary under paragraph (1) shall be made available to the public on the day it is so submitted, but no information which is described in section 552(b)(4) of title 5, United States Code, shall be included in the summary or otherwise released to the public.

''(e)(1) The Secretary shall request a nongovernmental scientific body to submit to the Secretary a list of names of persons, together with their qualifications, who such body believes to be qualified to serve on expert advisory panels appointed under subsection (f). Such list shall be revised on an annual basis.

''(2) Any person may submit to such nongovernmental body recommendations of persons to be included on the list submitted under paragraph (1).

(c) REPORT.—Not later than the expiration of one year from the date of the enactment of this Act, the Secretary of Health and Human Services shall report to the Congress on the Secretary's implementation of sections 505(i)(7) and 520(g)(6) of the Federal Food, Drug, and Cosmetic Act and the use the Secretary has made of institutional review boards. Such report shall include any difficulties the Secretary has encountered in the implementation of such sections and the use of institutional review boards.

SEC. 9. RATIONALIZING GOOD MANUFACTURING PRACTICES.

Section 501 (21 U.S.C. 351(a)) is amended—

(1) by inserting ''(A)'' after ''(a)(1)'' and redesignating ''(2)(A)'' as ''(B)(i)'', ''(B)'' as ''(ii)'' both times it appears, ''(3)'' as ''(C)'', ''(4)'' as ''(D)'', ''(5)'' as ''(E)'', ''(6)'' as ''(F)'', and ''(A)'' as ''(i)'' the second time it appears; and

(2) by inserting the following at the end of subsection (a):

''(B) The Secretary shall by regulation establish good manufacturing practices applicable to drugs subject to section 505 of this Act and biological products (other than blood, blood products and blood components, and vaccines that cannot adequately be characterized by physical or

chemical methods) subject to section 351 of the Public Health Service Act as follows:

''(i) One set of regulations shall apply only to drugs and biological products which cannot be characterized adequately by physical or chemical methods.

''(ii) A second set of regulations shall apply only to drugs and biological products which can be characterized adequately by physical or chemical methods.

''(C) Regulations established under subparagraph (B) shall establish requirements for submissions to the Secretary of changes in manufacturing practices by the applicant or holder. Such regulations shall provide as follows:

''(i) In the case of drugs and biological products which can adequately be characterized by physical or chemical methods, approval of manufacturing changes shall be required prior to implementation of such changes only if such manufacturing changes are specified in regulations as substantially affecting the safety or efficacy of such drugs and biological products.

''(ii) In the case of drugs and biological products which cannot be characterized adequately by

physical or chemical methods, approval of such manufacturing changes before implementation shall be required—

''(I) in the case of a drug or a biological product which is required under section 351(a)(1)(B) of the Public Health Service Act to have a product license, only if such manufacturing changes are specified in regulations as potentially affecting the safety or efficacy of such drug or biological product; or

''(II) in the case of a biological product which is subject to standards as determined under section 351(a)(1)(B) of the Public Health Service Act, only if such manufacturing changes are specified in the regulations as substantially affecting the safety, purity, or potency (or, in the case of tissue, safety, and integrity) of such biological products.

''(iii) Such regulations shall specify the types of manufacturing changes that must be submitted in writing to the Secretary (but not required to be approved prior to implementation). A request to make such changes must be submitted by the applicant or holder at least 30 days prior to implementation of such changes. Such request may be implemented on

the 31st day after submission unless on or before such day the Secretary disapproves such request and notifies the applicant or holder in writing of such disapproval. Such notification shall include a complete statement of the reasons for not allowing implementation.

''(iv) If upon further review, the Secretary identifies problems that would affect product safety, efficacy, purity, or potency or tissue integrity, the Secretary may disapprove the manufacturing changes. Taking into consideration risks involved, reasonable time shall be given the applicant or holder to comply with the disapproval.

''(v) A description of manufacturing changes not covered by clauses (i) or (iii) shall be submitted by the applicant or holder to the Secretary on an annual basis.

''(D)(i) The Secretary shall, after notice and opportunity for public comment pursuant to section 553 of title 5, United States Code, establish not later than December 31. 1998, regulations to be used in determining whether a drug or a biological product can adequately be characterized by physical or chemical methods.

''(ii) If the applicant disagrees with a determination by the Secretary that the drug or biological product which

is the subject of an application cannot be adequately characterized by physical or chemical methods, such applicant may contest such determination by requesting an informal hearing.

''(E) For purposes of subparagraphs (B) through (D)—

''(i) the term 'changes in manufacturing practices' means—

''(I) changes in manufacturing procedures generally applicable throughout the facility, such as changes in recordkeeping procedures, validation processes, methods of training of personnel, and methods of qualification of equipment;

''(II) changes in the manufacturing facility or equipment; and

''(III) changes in manufacturing procedures of specific applicability to a biological product;

''(ii) the term 'holder' means a person whose drug application submitted under section 505 or product license application submitted under section 351 of the Public Health Service Act has been approved; and

''(iii) the term 'applicant' means a person whose application described under clause (ii) has been submitted to, but not approved by, the Secretary.''.

SEC. 10. EXPORT OF DRUGS AND DEVICES.

(a) SECTION 801(e).—Section 801(e) (21 U.S.C. 381(e)) is amended—

(1) in paragraph (1), by inserting after ''under this Act'' the following: ''or in violation of section 505 or section 351 of the Public Health Service Act'';

(2) in paragraph (1), by amending subparagraph (B) to read as follows:

''(B) has been accepted or requested for import by the country to which it is intended for export and will be sold, tested, or otherwise used in such country'';

(3) in paragraph (1), by striking the last sentence;

(4) by amending paragraph (2) to read as follows:

''(2) Paragraph (1) does not apply to the export of—

''(A) any device—

''(i) which does not comply with an applicable requirement under section 514 or 515; or

''(ii) which under section 520(g) is exempt from either such section, or

''(B) any drug which does not comply with an applicable requirement under section 505 or 512 or section 351 of the Public Health Service Act,

unless the device or drug is in compliance with the requirements of paragraph (1) and if the device or drug is to be exported to a country which is not a member of the World Trade Organization, the person exporting it has notified the Secretary of the export at least 30 days before the export and has included in such notice the name of the product, the country to which the product is being exported and a brief description of the medical need for such device or drug in such country. In the case of a device or drug for which an export notice is required under this paragraph, the Secretary may prohibit the export of such device or drug if the Secretary determines that the possibility of the reimportation of the device or drug into the United States presents an imminent hazard to the public health and safety of the United States and the only means of limiting the hazard is to prohibit the export of the device or drug.''; and

(5) by adding the following at the end thereof:

''(f) The Secretary shall not exercise jurisdiction.—

''(1) over the labeling of drugs or devices intended for export in order to comply with requirements of foreign countries''; or

''(2) over drugs or devices not subject to subsection (e) which are intended for export and which are not intended for commercial sale or are intended for investigational use only.''.

(b) SECTION 802.—Section 802 (21 U.S.C. 382) is repealed.

SEC. 11. REGULATION OF BIOLOGICAL PRODUCTS.

Section 351(a) of the Public Health Service Act (42 U.S.C. 262(a)) is amended by inserting ''(1)(A)'' after ''(a)'' and by striking ''any virus'' and all that appears thereafter and inserting in lieu thereof the following: ''a biological product to which this section applies unless—

''(i) such biological product has been propagated, manufactured, or prepared in accordance with good manufacturing practices;

''(ii) such biological product is the subject of an approved product license or complies with a standard established by the Secretary; and

''(iii) each package of such biological product is plainly marked with the proper name of the biological product contained therein, the name, address, and establishment number of the manufacturer, and

the date beyond which the contents cannot be expected to yield their specific results.

''(B) The Secretary shall by regulation specify which biological products shall be required to have a product license or shall be subject to standards established under subparagraph (A)(ii), except that tissue, blood and blood components and derivatives (other than blood test kits) shall be subject to standards under paragraph (4).

''(2)(A) The Secretary shall establish, by regulation, requirements for product license applications. The Secretary shall approve a product license application upon a demonstration that there exists reasonable assurance that the biological product which is the subject of the application is safe and effective.

''(B)(i) The Secretary shall establish, by regulation, standards for biological products subject to such standards under paragraph (1)(B), except that tissue, blood, and blood components or derivatives (other than blood test kits) shall be subject to standards established under paragraph (4). Standards shall, as appropriate, reasonably assure the safety, purity, and potency of the biological product or class of biological products subject to such standard.

''(3)(A) A product license approved by the Secretary under paragraph (2)(A) and regulations established by the

Secretary under paragraph (2)(B) may require that lots or batches of a biological product be released only after certification that such lots or batches have the characteristics of safety, purity, and potency which the biological product purports or is represented to possess.

''(B)(i) A product license shall specify whether certification under subparagraph (A) will be by the manufacturer of the biological product, by the Secretary, or by a certified individual or independent laboratory under section 906 of the Federal Food, Drug, and Cosmetic Act.

''(ii) Certification of lots or batches by the Secretary or independent laboratory shall be required only for a period of not more than 6 months or until satisfactory history of consistent acceptable production has been established, which period will not be extended unless the Secretary determines in writing that continuing such certification is required to assure the safety and efficacy of the biological product.''.

''(iii) The Secretary may at any time, upon petition by the manufacturer or upon the Secretary's own initiative, terminate any requirement for certification.

''(4)(A) The Secretary shall by regulation establish standards for tissue, blood, and blood components or blood derivatives (other than blood test kits). Such standards shall assure the safety and integrity of the tissue, blood,

and blood components or derivatives (other than blood test kits). The Secretary shall solicit the submission of one or more proposed standards, applicable to tissue, blood, and blood components or derivatives (other than blood test kits) and approved by the Secretary as appropriate for purposes of this section, from professional and scientific organizations. The Secretary shall publish such standards as a notice of proposed rulemaking in accordance with paragraph (2)(B)(ii).

''(B) Tissue subject to this paragraph shall be processed in accordance with good manufacturing practices established by the Secretary under section 501.

''(C) The Secretary may use—

''(i) professional and scientific organizations, and

''(ii) accrediting bodies used to assure compliance with the standards of such organizations,

to assist in the implementation of subparagraph (A) and to assure that tissue meets the requirements of subparagraph (B).

''(D) For blood, blood products and blood components, and vaccines which cannot be adequately characterized by physical or chemical methods, the Secretary shall continue to implement the existing requirements for facilities where such blood, blood products, and blood compo-

nents are drawn processed, stored, or otherwise maintained for distribution or in which such vaccines are manufactured or propagated.

''(5) The requirements of paragraph (1) do not apply to a biological product—

''(A) for which there is in effect an investigational new drug application under section 505(i) of the Federal Food, Drug, and Cosmetic Act, or

''(B) for which there is in effect under paragraph (6) a provisional standards license.

''(6)(A) Each person who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a biological product which will require a standards license shall, at least 30 days before making such introduction or delivery submit to the Secretary (in such form and manner as the Secretary shall by regulation prescribe) a report that includes—

''(i) a description of the biological product;

''(ii) a statement of reasons satisfactory to the Secretary that the biological product will require a standards license (and not a product license);

''(iii) assurances by such person which are satisfactory to the Secretary that such biological product will be manufactured in accordance with good

manufacturing practices described in paragraph (1)(A)(i); and

''(iv) such other information as the Secretary may by regulation require.

''(B) Upon the expiration of 30 days after the receipt by the Secretary of a report under subparagraph (A), the biological product for which the report was submitted shall be deemed to have a provisional standards license unless before the expiration of such days the Secretary determines that a requirement of such subparagraph (A) has not been met. If the Secretary determines that such a requirement has not been met, the Secretary shall provide to the person who submitted the report on which such determination was made an opportunity for an informal hearing.

''(C) A provisional standards license under subparagraph (A) shall expire upon the issuance of a standards license under paragraph (2).

''(7) For purposes of this subsection—

''(A) the term 'tissue' means a collection of human cells which are similar or the intercellular substances surrounding them, or both, which—

''(i) are intended for administration to a human being for the diagnosis, cure, mitigation,

treatment, or prevention of any disease or condition;

''(ii) are procured, processed, stored, or distributed by methods to prevent the transmission of infectious disease and to preserve or enhance clinical usefulness;

''(iii) may be processed to remove some of its constituents but have not been modified chemically;

''(iv) may be combined with substances such as excipients, fillers, or carriers that are not devices or pharmacologically active;

''(v) if subjected to expansion, manipulation, or other processing (which may include modification of physical form or structure) before being transplanted or implanted, are not thereby substantially altered in their inherent structural or functional characteristics; and

''(vi) achieve their principal intended purposes through structural or functional support and not systemic action;

but such term does not include vascularized human organs.

''(B) the term 'biological product to which this section applies' means a virus, therapeutic serum,

toxin, antitoxin, tissue, blood, component or derivative, allergenic biological product, or an other analogous biological product or arsphenamine or its derivative applicable to the prevention, treatment, or cure of diseases or conditions of human beings.''.

SEC. 12. INITIAL REPORTING OF DEVICES.

(a) CLASS I DEVICES.—Section 510(k) (21 U.S.C. 360(k)) is amended by adding after paragraph (2) the following: ''No person shall be required to make a report under this subsection with respect to a class I device or a class II device which the Secretary has designated after notice and comment rulemaking to be exempt from such requirement.''.

(b) RULEMAKING.—Within 30 days of the date of the enactment of this Act, the Secretary of Health and Human Services shall publish a notice requesting identification of class II devices which should be placed in class I. Upon the expiration of 30 days after the date of such notice, the Secretary shall publish a proposal to exempt from the notification required under section 510(k) of the Federal Food, Drug, and Cosmetic Act the class II devices identified in response to the notice. Within 60 days of such publication, the Secretary shall publish a final regulation exempting the specified class II devices from such notification requirement. If the Secretary does not publish a final

regulation, the devices contained in the proposed regulation shall be deemed exempt from such notification requirement.

(c) DEVICE MODIFICATIONS.—Section 510(k) (21 U.S.C. 360(k)), as amended by subsection (a), is amended by adding at the end the following: ''A person who modifies a device in such a manner that has no substantive effect on the character, utility, or therapeutic nature of the device shall not be required to make a report under this subsection because of such modification and shall maintain data or information that demonstrates that a report under this subsection is not required in such person's good manufacturing practice document file. Such data or information shall be available upon request to the Secretary.''.

SEC. 13. FDA RESPONSE TO G.M.P. VIOLATIONS.

Section 520(f) (21 U.S.C. 360j) is amended by adding at the end the following:

''(4) The Secretary may not delay the approval of a device under a section 510(k) report because the person who made the report is in violation of a requirement prescribed under paragraph (1) unless the Secretary determines that the violation is reasonably related to such device or is related to all the operations of such person. If the Secretary delays such approval because of such a viola-

tion, the Secretary shall, within 60 days of being notified that corrective actions have been taken, reinspect for such violations or remove the delay. The Secretary shall prepare information for persons making reports under section 510(k) to inform them of the provisions of this paragraph.''.

○

HR 1742 IH——2

HR 1742 IH——3